UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,531	03/15/2004	Samuel Achilefu	073979.39.C1	2309

27805 7590 07/24/2008

THOMPSON HINE L.L.P.
Intellectual Property Group
P.O. BOX 8801
DAYTON, OH 45401-8801

EXAMINER	
JONES, DAMERON LEVEST	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
07/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,531	ACHILEFU ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/29/08 & 3/30/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-35 and 45-50* is/are pending in the application.

4a) Of the above claim(s) *46-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-35 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 3/3/08 wherein claim 32 was amended; claims 1-31 and 36-44 were canceled; and claims 45-50 were added. In addition, the Examiner acknowledges receipt of the request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/29/08 has been entered. Also, the Examiner acknowledges receipt of the acceptable terminal disclaimer filed 3/30/08.

Note: Claims 32-35 and 45-50 are pending.

RESPONSE TO APPLICANT'S AMENDMENT/ARGUMENTS

2. The Applicant's arguments and/or amendment filed 3/30/08 to the rejection of claims 32-35 made by the Examiner under 35 USC 103 and/or double patenting have been fully considered and overcome for the reasons set forth below.

Double Patenting Rejection

The double patenting rejection is WITHDRAWN because Applicant has filed an acceptable terminal disclaimer.

103 Rejections

I. The 103(a) rejection over Eversole et al is WITHDRAWN.

II. Applicant's arguments with respect to claims 32-35 have been considered but are moot in view of the new ground(s) of rejection.

Note: Applicant's arguments will be addressed in the new grounds of rejection below.

CLARIFICATION OF RECORD

3. Applicant's election of the organic solvent, DMSO (dimethylsulfoxide), in the response filed 7/9/07 is once again noted. Thus, the prior art was re-evaluated with DMSO as the solvent. The search was not further expanded because prior art was found which could be used to reject Applicant's claims.

WITHDRAWN CLAIMS

4. Claims 46-50are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention/species.

NEW GROUNDS OF REJECTIONS

112 First Paragraph Rejection (Scope of Enablement)

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 32-35 and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cyanine dyes of Formulae 1, 2, 3, and 4 (see specification), does not reasonably provide enablement for all photodiagnostic and phototherapeutic dyes which may be administered to a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are (1) nature of the invention; (2) state of the prior art; (3) level of one of ordinary skill in the art; (4) level of predictability in the art; (5) amount of direction and guidance provided by the inventor; (6) existence of working examples; (7) breadth of claims; and (8) quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(1) Nature of the invention

The claims are directed to a method of enhance fluorescence of a dye by adding a biocompatible organic solvent at a concentration ranging from about 1% to about 50% to enhance dye fluorescence during the photodiagnostic or phototherapeutic procedure.

(2) Level of one of ordinary skill in the art

The level of one of ordinary skill in the art is high because Licha et al (US Patent No. 6,083,485, column 3, lines 1-10) disclose that cyanine dyes may be used as photographic layers and such dyes need not have *any* luminescent properties. As a result, cyanine dyes with fluorescent properties were synthesized for use in fluorescence microscopy. Thus, independent claim 32 encompasses a vast number of dyes. Applicant's specification does not enable the public to make or use such a vast number of possible dyes, other than cyanine dyes of Formulae 1, 2, 3, and 4 as set forth in the instant invention.

(3) Level of predictability in the art

The art pertaining to the cyanine dyes is highly unpredictable. For example, Licha et al disclose that some cyanine dyes do not have any luminescent properties (see US Patent No. 6,083,485, column 3, lines 1-10). Thus, determining the various types of dyes or class of dyes that are compatible with the instant invention requires various experimental procedures and without guidance that is applicable to all cyanine dyes, there would be little predictability in performing the claimed invention.

(4) Amount of direction and guidance provided by the inventor

Independent claim 32 encompasses a vast number of dyes. Applicant's limited guidance does not enable the public to prepare such a numerous amount of dyes. Furthermore, there is no directional guidance for the dyes other than those of Formulae 1, 2, 3, or 4 that will have enhanced fluorescence in the presence of a biocompatible organic solvent. Hence, there is no enablement for all possible permutations and biocompatible organic solvent combinations.

(5) Breadth of claims

The claims are extremely broad due to the vast number of possible dyes and biocompatible organic solvents known to exist.

(7) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with the claims. In particular, the specification fails to enable the skilled artisan to practice the invention without undue

experimentation. Furthermore, based on the unpredictable nature of the invention, and the extreme breadth of the claims, one skilled in the art could not perform the claimed invention without undue experimentation.

112 Second Paragraph Rejections

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 32-35 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims as written are ambiguous because it is unclear what dyes other than those disclosed in the specification, cyanine dyes of Formula 1, 2, 3, and 4, Applicant is claiming that are compatible with the instant invention.

103 Rejection

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 32-35 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Licha et al (US Patent No. 6,083,485) in view of Song et al (Journal of Chemical Physics, 1996, Vol. 104, No. 21, pages 8230-8236).

Licha et al disclose dyes which may be administered in vivo and radiates in the near infrared radiation region. The fluorescence dyes (e.g., cyanine dyes) may be used for various diagnostic purposes (see the entire document, especially, abstract; column 4, lines 6-28; columns 4-5, bridging paragraph; column 6, lines 17-45; columns 6-7, bridging paragraph). The compounds of Licha et al are water soluble, tolerable, and stable in vitro and in vivo (column 8, lines 31-37). The dye mixture may be administered by intravenous injection and they irradiated with light (column 8, lines 42-49). In addition, Licha et al disclose that for cyanine dyes, increased solubility in water and the presences of hydrophilic groups suppress the formation of aggregates and micelles

(column 13, lines 15-22). The dye compositions may optionally contain common adjuvants, diluents, electrolytes, buffers, and substances such as cyclodextrin (column 14, lines 37-52). Example 2, column 15, disclose the making of a dye composition wherein a cyanine dye is added to an organic solvent, isopropanol, and crystals allowed to precipitate. In Example 6, columns 16-17, the ethanol is added to the dye and a precipitate is allowed to form. Licha et al fail to disclose that the dye is combined with the biocompatible organic solvent during the photodiagnostic or phototherapeutic procedure. In addition, Licha et al fail to disclose the specific concentration of the organic solvent.

Song et al disclose dicarbocyanine dyes in organic solvents such as methanol, 2-propanol, and DMSO. In particular, the fluorescence data obtained by Song et al disclose that the cyanine dyes had the greatest fluorescence in DMSO, by the results obtained by 2-propanol and methanol were comparable to those obtained from DMSO (see entire document, especially, abstract; page 8230, see entire document; page 8231, left column, first complete paragraph; pages 8231-8232, bridging paragraph; page 8232, left and right column, bridging paragraph; page 8232, Figure 1; page 8233, Table I; and pages 8235-8236, bridging paragraph).

It would have been obvious to one of ordinary skill in the art to use DMSO as the biocompatible organic solvent because it is disclosed in the art, as illustrated in Song et al, that the presence of a cyanine dye in combination with DMSO results in enhance fluorescence. For example, Song et al disclose (see Table 1, page 8233) disclose cyanine dyes in the presence of three biocompatible solvents (2-propanol, methanol,

and DMSO) and the greatest fluorescence enhancements were observed when the dyes were placed in DMSO. Hence, it would have been obvious to one of ordinary skill in the art to combine a cyanine dye with DMSO. Furthermore, since Licha et al disclose that that the dyes may be used for in vivo diagnostics using near infrared radiation optional with common adjuvants, diluents, buffers, cyclodextrin, etc. (column 14, lines 37-51), a skilled artisan would be motivated to use various organic solvents. However, since the prior art the use of solvents such as methanol, 2-propanol, and DMSO (see Song et al, Table 1, page 8233) and Licha et al disclose organic solvents such as isopropanol (see Example 2, column 2), the reference teachings were combined. A skilled artisan would be motivated to optimize the range of the concentration of the biocompatible organic solvent given the general information as set forth in Song et al regarding the fluorescence data and the desire to obtain the maximum fluorescence. Also, Licha et al disclose (column 9, lines 1-6) disclose that methods are known to a skilled artisan as to what equipment parameters should be set to obtain optimum recording and evaluation conditions at given absorption or fluorescence wavelengths of the dyes.

Since both Licha et al and Song et al disclose cyanine dyes which may be combined with organic solvents, the references may be considered to be within the same field of endeavor. Therefore, the reference teachings are combinable.

Previously, Applicant asserted that Licha et al do not disclose adding an organic solvent that is administered to a patient. Instead, Applicant's position is that Licha et al adds an organic solvent pre-administration to a patient, to determine dye equilibrium

properties. As a result, Applicant has concluded that the reference does not teach, suggest, or motivate used in a patient to enhance fluorescence. Furthermore, Applicant asserts that fluorescence enhancement is not required for the process of equilibrium partitioning.

First, it is noted that the claims do not exclude adding a biocompatible solvent prior to administration to a subject to the dye. Secondly, since a composition is inseparable from its properties, if both Applicant and the cited prior art disclose adding a dye to a biocompatible organic solvent, then the properties will be similar regardless of whether the biocompatible organic solvent is added later. It is duly noted that no evidence has been made of record to indicate that different results are obtained if a dye is added to during the photodiagnostic or phototherapeutic procedure as opposed to during the making of the composition. Furthermore, a skilled artisan would recognize that while the examples of Licha et al disclose combining the dye and biocompatible organic solvent and later allowing a precipitate to form, the skilled artisan would recognize that the crystal would be reconstituted if the composition is used for in vivo use. For example, in column 8, lines 31-37 and 42-44, it is disclosed that the composition may be administered intravenously. Also, in column 3, lines 35-44, it is disclosed that the dyes should meet the requirements that generally apply to diagnostic pharmaceuticals. Also, since Song et al disclose enhanced fluorescence in the presents of some organic solvents, a skilled artisan would be motivated to reconstitute solid dye compounds of Licha et al with and organic solvent (e.g., DMSO) for in vivo use because of the enhanced fluorescent results disclosed in Song et al. Licha et al further

disclose that dyes suitable for diagnostic purposes should be soluble in water and sufficiently stable in chemical and photophysical respect for at least as long as the diagnostic period lasts.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/D. L. Jones/
Primary Examiner
Art Unit 1618

July 18, 2008